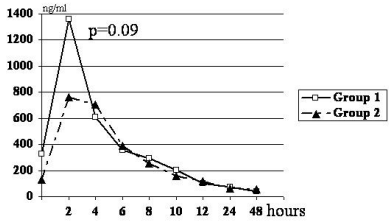

Figure 1. Serial measurements of plasma myoglobin levels

POSTER SESSION

1012 Heart Failure: Chronic Treatment

Sunday, March 07, 2004, 9:00 a.m.-11:00 a.m.
Morial Convention Center, Hall G
Presentation Hour: 10:00 a.m.-11:00 a.m.

1012-103 Blood Pressure Changes Do Not Influence the Beneficial Effects of Carvedilol Compared to Metoprolol in the Patients With Heart Failure: Results From COMET (Carvedilol or Metoprolol European Trial)

Marco Metra, Andrea Di Lenarda, Peter Hanrath, Michel Komajda, Beatrix Lutiger, John G. Cleland, Willem J. Remme, Armin Scherhag, Andrew Charlesworth, Karl Swedberg, Christian Torp-Pedersen, For the COMET investigators, University of Brescia, Brescia, Italy, National Heart and Lung Institute, London, United Kingdom

Background: The Carvedilol or Metoprolol European Trial (COMET) has shown a reduction in all-cause mortality with carvedilol, compared with metoprolol, in 3029 patients with chronic heart failure (RR 0.83, 95%CI, 0.74-0.93, p=0.0017). The potenital influence on this difference of effects on blood pressure (BP) is unknown.
Methods: We have related the effects on long-term mortality of baseline BP and its early changes (Δ) in COMET. Baseline analyses are presented for the intent to treat population. ΔBP analyses are on treatment.
Results: At the end of the uptitration phase, 4 months after randomization, mean systolic BP (SBP) declined from baseline by 3.8 ± 17.4 mm Hg in the carvedilol group and 2.0 ± 17.7 mm Hg in the metoprolol group (p = 0.01). Patients on carvedilol maintained a significantly lower mean SBP at most visits and also had a lower mean diastolic BP (DBP) at 4, 8, 16, 32, 44 and 52 months. Among the 2589 patients reassessed at 4 months, ΔSBP ≤ -3 mm Hg (median value) was found in 685/1291 (53%) patients on carvedilol and in 617/1298 (48%) on metoprolol. Compared with the others, the patients with a ≥ -3 mm Hg ΔSBP had a higher baseline SBP (133±19 versus 121±17 mm Hg, p<0.001) and DBP (79±11 versus 76±10 mm Hg, p<0.001) with an higher prevalence of ischemic heart disease (54% versus 48%, p=0.002) and a lower prevalence of idiopathic cardiomyopathy (43% versus 49%; p=0.001) and diabetes (21% versus 26%; p=0.002). There were 409/1302 deaths (31%) in the patients with a ΔSBP ≥ -3 mm Hg and 400/1287 (31%) in the others. Mortality was reduced with carvedilol, compared to metoprolol, both in the patients with ΔSBP ≥ -3 mm Hg (28% versus 36%; RR, 0.76, 95% CI, 0.62-0.92; p=0.0049) and in the others (28% versus 34%; RR, 0.79; 95% CI, 0.65-0.97; p=0.0229). No interaction between the effect on mortality of carvedilol, compared to metoprolol, and the ΔSBP was found (RR 1.05; 95% CI, 0.80-1.39). By multivariate analysis, a SBP >120 mmHg at baseline was associated with a lower mortality (RR, 0.72; 95% CI, 0.63-0.83; p<0.0001) while ΔSBP was not significant.
Conclusion: Carvedilol reduces mortality compared to metoprolol irrespective of BP lowering. A higher baseline SBP is associated with a lower mortality risk.

1012-104 Safety of Beta-Blockers in Patients With Heart Failure and Renal Insufficiency: Data From IMPACT-HF

Adrian F. Hernandez, Wendy A. Gattis, Jyotsna Garg, Alan Chu, A. Bleakley Chandler, Mihai Gheorghiade, Christopher M. O'Connor, Duke Clinical Research Institute, Durham, NC

Background: Renal insufficiency is a significant predictor of poor outcomes in heart failure (HF) patients. To date, little is known about the safety of beta-blockers (BB) in heart failure patients with renal insufficiency because clinical trials of BB excluded patients with significant renal disease.
Methods: The IMPACT-HF study was conducted in patients with systolic dysfunction admitted for worsening chronic HF symptoms. The trial randomized patients to in-hospital initiation of carvedilol compared to the standard practice of post discharge (>2 weeks) BB initiation. A registry was conducted concurrently with the main trial to collect data on all HF hospitalizations. The IMPACT-HF trial and registry databases were combined and retrospectively analyzed to determine if the use of BB in HF patients with moderate (estimated GFR 30-60 mL/min per 1.73 m2) or severe (<30 mL/min per 1.73 m2) renal insufficiency had a higher rate of death or rehospitalization within 60 days than patients without beta-blockers. An unadjusted analysis was performed, as well as a model adjusted for age, systolic blood pressure at baseline and nitrates prescribed at admission and prior HF hospitalizations.
Results: Overall, 908 pts were enrolled in the IMPACT-HF trial and registry. In the total population, 270 (29.7%) pts had severe renal insufficiency and 308 (33.9%) pts had moderate renal insufficiency. Degree of renal insufficiency significantly correlated with 60-day death and rehospitalization- severe 37.4%; moderate 33.4%; normal 18.2% (p <0.01). There were 531 pts with BB and 377 pts without a BB on discharge. In a risk-adjusted model, there was no adverse effect of BB use in patients with moderate or severe renal insufficiency (wald chi-sqr =0.0748; p= 0.7845).
Conclusions: Beta-blockers may be safely used in HF patients with renal insufficiency. Beta-blocker use does not appear to cause early worsening HF requiring rehospitalization even in patients with moderate or severe renal insufficiency.

1012-121 Lack of Heart Rate Effects on the Mortality Benefits of Carvedilol Compared to Metoprolol in the Patients With Heart Failure: Results From the Carvedilol or Metoprolol European Trial (COMET)

Marco Metra, John G. Cleland, Andrea Di Lenarda, Peter Hanrath, Michel Komajda, Beatrix Lutiger, Philip A. Poole-Wilson, Willem J. Remme, Armin Scherhag, Andrew Charlesworth, Karl Swedberg, Christian Torp-Pedersen, For the COMET investigators, University of Brescia, Brescia, Italy, National Heart and Lung Institute, London, United Kingdom

Background: The Carvedilol or Metoprolol European Trial (COMET) has shown a reduction in all-cause mortality with carvedilol, compared with metoprolol, in 3029 patients with chronic heart failure (RR 0.83, 95%CI, 0.74-0.93, p=0.0017). The potential influence on this difference of effects on heart rate (HR) are unknown.
Methods: We related the effects on long-term mortality of baseline HR and early changes (Δ) of HR in COMET. Baseline analyses are presented for the intent to treat population, ΔHR analyses are on treatment.
Results: At the end of uptitration, 4 months after randomization, mean HR declined from baseline by 13.3 beats per minute (bpm) in the carvedilol group and 11.7 bpm in the metoprolol group (difference -1.6 bpm; 95%CI, -2.7 to -0.6). Patients on carvedilol maintained a significantly lower mean HR only at two more visits (8, 16 months). Among the 2579 patients reassessed at 4 months, Δ HR ≥ -12 bpm (median value) was found in 714/1289 (55%) patients on carvedilol and in 640/1290 (50%) patients on metoprolol (p=0.0033). Compared with the others, the patients with a ≥ -12 bpm ΔHR had a higher baseline HR (87±13 versus 75±11 bpm, p<0.001) and a lower LVEF (25.6±7 versus 26.7±7% p<0.001) with a lower percentage of males (78% versus 82%, p=0.0082) and of patients with a pacemaker (2.6% versus 9.1%; p<0.001) and a higher percentage in sinus rhythm (78.5% versus 73.2%; p=0.0017). Within each subgroup, the HR profiles were the same for carvedilol and metoprolol. Mortality was the same (31%) in the patients with a ΔHR ≥ or < -12 bpm. Mortality was reduced with carvedilol, compared to metoprolol, both in the patients with ΔHR ≥ -12 bpm (28% versus 35%; RR 0.77, 95% CI, 0.64-0.94; p=0.0086) and in the others (28% versus 34%; RR 0.79; 95% CI, 0.65-0.97; p=0.0229). No interaction between the effect on mortality of carvedilol, compared to metoprolol, and the ΔHR was found (RR 1.021; 95% CI, 0.77-1.35). By multivariate analysis, neither the baseline HR nor ΔHR were associated with mortality.
Conclusion: Outcome is not directly or simply related to baseline HR or its early changes in COMET.

1012-122 Chronic Treatment With Carvedilol Improves Left Ventricular Pump Performance by Increasing Intrinsic Myocardial Contractility in Patients With Heart Failure

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Background: Chronic treatment with β-blockers improves LV pump performance in patients with heart failure (HF); however, it is not known whether this improvement is related to changes in LV remodeling, LV loading conditions or intrinsic myocardial contractility. Accordingly, the **purpose** of this study was to study mechanisms of improvement in LV pump performance following β-blocker treatment in HF patients. **Methods:** 32 patients with HF, LVEF<35 %, NYHA Class II-IV, on ACE inhibitors but not on β-blockers were studied at baseline and at 6 months after treatment with carvedilol. Cardiac output (CO), LV fractional shortening (FS), velocity of circumferential fiber shortening (VCF)- relatively afterload dependent measures of contractility, LV end systolic stress (LVESS),VCF:LVESS relation –an afterload corrected measure of contractility, LV end diastolic volume (LVol), and LV mass (LVM) were measured by echocardiography and LVEF by MUGA. **Results:** Carvedilol treatment resulted in significant (p 0.01-0.04) improvements in load independent (VCF:LVESS ratio), and load dependent indices of contractility (FS,VCF, LVEF), as well as a decrease in LV end-diastolic volume.(Table) There were no significant changes in LV end-systolic stress or in LV mass. **Conclusions:** Taken together these studies suggest that the improvements in LV pump performance after chronic treatment with carvedilol are multifactorial and are related to changes in intrinsic myocardial contractility as well as changes in LV preload.